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INVESTMENT HIGHLIGHTS

- Sensorion is focused on **innovative treatments** that can **restore, treat** and prevent hearing loss
- Three novel gene therapy programs targeting unmet needs in Otoferlin Deficiency, GJB2-related hearing loss and Usher Syndrome Type 1
 - Promising pre-clinical data demonstrating improvement and restoration of hearing and vestibular functions (OTOF/USH1)
- Exclusive relationship with Institut Pasteur for all Inner Ear Gene Therapy Programs during the timeframe of the agreement
- Phase 2 study for Sudden Sensorineural Hearing Loss with an oral small molecule
 - Global, randomized study with data expected in Q4 2021
- Experienced management team with broad expertise in gene therapy and drug development
- Strong shareholder support from **leading blue-chip investors**



FINANCIALOVERVIEW

Date Established	
IPO	2015
Euronext Paris	ALSEN.PA
Cash (Dec 31, 2020):	€62.2m
Cash runway until end of H2 2022	

SENSORION

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MANAGEMENT TEAM



NAWAL OUZREN Chief Executive Officer

> SENSORION (Since 2017)

SHIRE (2016-2017) Head of the Global Genetic Diseases Franchise

BAXALTA (2014-2016) Vice President of the Global Hemophilia Franchise

> BAXTER (2006-2014) Vice President



GÉRALDINE HONNET Chief Medical Officer

> SENSORION (Since 2020)

GENETHON (2011-2020) Director of Development

TRANSGENE (2007-2011) Responsible of development of infectious diseases programs

JANSSEN-CILAG EMEA (2005-2007) European Project Manager Virology

PAREXEL INTERNATIONAL (2001-2005) Medical Director



NORA YANG Chief Scientific Officer

> SENSORION (Since 2021)

STRATIFY (2020-2021) Cofounder and CSO

NIH (2010-2019) Director of portfolio management and strategic operations

AMGEN (2004-2006) Sr Global Project Manager

ELI LILLY (1992-2004) Project team leader, new drug discovery



OTMANE BOUSSIF Chief Technical Officer

> SENSORION (Since 2021)

NOVARTIS (Since 2015) Head Cell & Gene Therapy T. Dev.

SANOFI (Since 2006) Director Purification & Formulation processes, vaccines

> MERCK SERONO (Since 2004) Manager Pre-formulation downstream processing

> > **AVENTIS**

(Since 2000) Manager Formulation & Precliniical manufacturing

SENSORION

Sensorion is building up a gene therapy franchise in collaboration with Institut Pasteur

- Management team highly experienced in gene therapy and drug development
- **RESTORE**, **TREAT** and **PREVENT** in the field of hearing loss: Phase 2 small molecule and new focus on gene therapies
- High profile collaborations and partners attracted high profile investors:
 - Institut Pasteur, Cochlear[®], French Armed Forces Biomedical Research Institute (IRBA) and Necker Hospital
 - ~€69.1m raised with key investors including Invus, Sofinnova Partners, Wuxi Apptec and 3SBio

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STRATEGY: **RESTORE**, **TREAT** & **PREVENT** HEARING LOSS



GENE THERAPY APPROACH

- Exclusive collaboration signed with Institut Pasteur in Gene Therapy to **RESTORE** auditory functions
- Program to RESTORE hearing in Otoferlin deficiency (DFNB9 deafness), one of the most common forms of congenital deafness
- Program to RESTORE hearing in GJB2-related hearing loss, the most common form of congenital deanfess, also involved in adult early onset forms of severe presbycusis and in childhood onset forms of hearing loss
- Program to **RESTORE** hearing in Usher Syndrome Type 1

SMALL MOLECULE APPROACH

- Phase 2 PoC study ongoing with SENS-401 to TREAT Sudden Sensorineural Hearing Loss
- Pre-clinical study completed with SENS-401 to **PREVENT** cell death following cochlear implant procedure.
- SENS-401 to PREVENT Cisplatin-induced Ototoxicity

SENSORION FORMED CRITICAL STRATEGIC ALLIANCES FROM BENCH TO BEDSIDE



INSTITUT PASTEUR IS LEADING THE WAY IN THE GENETICS OF HEARING



CHRISTINE PETIT MD, PhD

- Chair of Genetics and Cellular Physiology, Professor at College de France
- Professor at Institut Pasteur (Paris)
- Head of the Laboratory of Genetics and Physiology of Hearing at Institut Pasteur
- Founding Director of the French Hearing Institute
- Chair of the Scientific Advisory Board at Sensorion

Awards and Distinctions

- Louisa Gross Horwitz Prize
- Kavli Prize in Neuroscience
- ARO Lifetime Achievement Award of Merit
- International Brain Prize from Grete Lundbeck Foundation
- Hughes Knowles Prize
- Louis-Jeantet for Medicine Prize
- L'Oréal-UNESCO for Women in Science Award
- Inserm Grand Prix
- Member of the French and American Sciences Academies and the American Medical Academy



GENETICS AND PHYSIOLOGY OF HEARING UNIT AT INSTITUT PASTEUR LED BY PROFESSOR CHRISTINE PETIT

- >300 publications
- Mapped the first 2 genes (GJB2 and MYO7A) underlying childhood autosomal recessive deafness
- Identified more than 20 causative genes of hearing impairment
- Developed an interdisciplinary approach involving study of mouse models of various forms of human deafness as well as cell- and temporal-specific conditional KO mice
- Unraveled the pathogenic processes of a large spectrum of deafness

https://research.pasteur.fr/en/team/genetics-physiology-of-hearing/

SENSORION HAS ENTERED INTO A BROAD STRATEGIC R&D COLLABORATION WITH INSTITUT PASTEUR ON GENETICS OF HEARING

SENSORION HAS A RIGHT OF FIRST REFUSAL ON ALL GENE THERAPY PROGRAMS IN THE FIELD OF INNER EAR AT INSTITUT PASTEUR



SCIENTIFIC ADVISORY BOARD



Pr Christine Petit Chair of the Scientific Advisory Board



Pr Alain Fischer

- Professor at College de France
- 2009-2016: Director and Founding Member of the Institute for Genetic Diseases (Imagine)
- 1996-2012: Director of the pediatric immunology department at Necker Hospital
- Pr Fischer notably led pioneering research on gene therapy



• ENT Surgeon

- Principal Associate Investigator at the Hearing Institute (Paris)
- Currently pursuing research on deciphering language processing variability in deafness



Dr Hernán López-Schier

- Senior Group Leader and Research Unit Director at the Helmholtz Center (Munich)
- Currently pursuing research on fundamental sensory biology and sensory dysfunction
- His group was the first to visualize the regeneration of mechanosensory hair cells in their natural context



Pr Paul Avan

- Physicist and Medical Doctor in Biophysics
- Head of the Center for Research and Innovation in Human Audiology at Hearing Institute (Paris)
- Designed original objective methods of exploration of the cochlea and auditory pathways



Dr Rob Dow

- >37 years of experience in the pharmaceutical and biotech industry
- Former Chief Medical Officer at PPD Inc.
- Substantial experience across therapeutic areas from preclinical to Phase 3 development

THE INNER EAR IS ONE OF THE MOST DELICATE ORGANS IN THE HUMAN BODY



ACCORDING TO THE WORLD HEALTH ORGANIZATION*:

~1.5bn PEOPLE AFFECTED BY HEARING LOSS WORLDWIDE

~2.5bn PEOPLE PROJECTED TO BE AFFECTED BY 2050

KEY FACTS

- Every human is born with a specific number of sensory hair cells
 - 3,500 Inner Hair Cells
 - 12,000 Outer Hair Cells
 - Hair cells do not naturally regenerate

*2021 WHO World report on Hearing

PIPELINE: BUILDING AN ATTRACTIVE PIPELINE IN THE HEARING SPACE

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	Product	Indication	Discovery	In vivo PoC	Pre-clinical	Phase 1	Phase 2	Phase 3	Next milestones (estimated timelines)
TREAT	SENS-401	Sudden sensorineural hearing loss							Phase 2 topline results (Q4 2021)
	SENS-401	Cisplatin induced ototoxicity							Start of natural history clinical study (mid-year 2021)
PREVENT	SENS-401	Hearing preservation after cochlear implantation			Cochlear"				Cochlear and Sensorion to begin first clinical trial
	SENS-401	Aminoglycoside induced ototoxicity							
	OTOF-GT*	Otoferlin deficiency							Discussion with reg. authorities (mid-year 2021)
ш	Usher-GT*	Usher syndrome Type 1							Pre-clinical Confirmatory PoC studies (mid-year 2021)
ESTOR	GJB2-GT*	GJB2-related early presbycusis							Candidate selection
₩	GJB2-GT*	Pediatric progressive GJB2- related hearing loss							Candidate selection
	GJB2-GT*	Congenital GJB2- related hearing loss							Candidate selection

3SBio has a right of first refusal with respect to licensing in Greater China of SENS-401 (except in combination with cochlear implants), OTOF-GT and USHER-GT *Option to obtain a licence from Institut Pasteur (pre-defined financial terms and other terms to be negotiated)

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GENE THERAPY RESTORE

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RESTORE

SENSORION'S FIRST GENE THERAPY PROGRAMS TO TREAT RARE AUDITORY DISEASES

3 PROGRAMS INITIATED UNDER THE STRATEGIC COLLABORATION AGREEMENT WITH INSTITUT PASTEUR

OTOFERLIN DEFICIENCY	GJB2-RELATED HEARING LOSS	USHER SYNDROME TYPE 1
Patients with mutations in OTOF suffer from severe to profound sensorineural prelingual non-syndromic hearing loss	 We have identified three forms of hearing loss associated with GJB2 gene mutations: Early onset of severe presbycusis Childhood onset 	Patients with Usher Syndrome Type 1 are born with severe to profound congenital bilateral sensorineural hearing loss and congenital vestibular dysfunction. Progressive vision loss
Otoferlin deficiency could be responsible for up to 8% of all cases of congenital hearing loss Prevalence $\sim 20,000$ in the USA + EU	 Congenital onset ~100,000 patients between 30 and 69 years old thought to be affected by a monogenic form of presbycusis due to GJB2 mutations 	appears during childhood Prevalence of Usher Syndrome: 4-17 per 100,000 people (~13k-55k patients in EU5 countries; ~13k- 56k patients in USA)
Incidence ~1100 per year in USA + EU	 Prevalence of congenital and childhood onset forms are estimated to be around 200,000 patients as around 50% of autosomal recessive non syndromic hearing loss cases are thought to be from GJB2 mutations 	Usher Syndrome Type 1 represents ~40% of all cases of Usher Syndrome We are addressing the USH1G mutations

burces: Akil *et al.* 2019 (link), Orphanet (link), NIH (link), company estimates based on publicly available population data, Chardan 2020 report, Bryan, Garnier & Co 2019 report Institut Pasteur, Boucher *et al.* 2020 (link)

DELAYED DIAGNOSIS – NOT SUSPECTED AT FIRST SIGHT

GENE THERAPY HAS A LIFE-CHANGING POTENTIAL FOR THESE AUDITORY DISEASES

OTOF GENE ENCODES OTOFERLIN, A KEY CA²⁺ SENSOR PROTEIN



Model illustrating calcium regulation of otoferlin/SNARE interaction in the hair cell. – Adapted from Ramakrishnan et al. 2014

OTOF is the gene coding for the Otoferlin protein, a Ca2⁺ sensor for vesicle fusion and vesicle pool replenishment at auditory hair cell ribbon synapses

RESTORE

DUAL AAV OTOF GENE THERAPY -MECHANISM OF ACTION



RESTORE

PRE-CLINICAL OTOF GENE THERAPY PROOF OF CONCEPT DURABLY RESTORES COCHLEAR RECEPTOR FUNCTION IN A KNOCK-OUT MOUSE MODEL

Immunostained inner hair cells in wild type, Otof -/- and Otof -/- injected with dual AAV2 quadY-F OTOF vector expression of Otof protein in cochlear receptors





Akil et al. 2019 (link)

OTOFERLIN "AUDINNOVE" CONSORTIUM PROVIDES PRIVILEGED ACCESS TO PATIENTS AND SURGEONS

Audinnove consortium received Hospital-University Research (RHU) prize:

- The consortium is eligible to receive up to €9.7m to develop a gene therapy program addressing Otoferlin deficiency
- Natural history: clinical evaluation and selection of patients
- Database compilation with genotypic and phenotypic characterization of children with congenital hearing loss
- Phase 1 gene therapy study (financing up to 1st patient in the clinical study)

This consortium is key to the understanding of the epidemiology and to build awareness of the emerging gene therapies

Necker-Enfants Malades Hospital

- The first dedicated pediatric hospital in the world
- Today one of the largest children's hospital in Europe

The Reference Center for Genetic Deafness at Necker coordinates the French and European genetic deafness networks



This project is financed by the French state, via the National Research Agency through the "Investing for the future" program (ref: ANR-18-RHUS-0007)

AUDINNOVE CONSORTIUM MEMBERS Sensorion INSTITUT PASTEUR Necker HÔPITAL UNIVERSITAIRE FONDATION POUR L'AUDITION OUTE DE

OTOF GENE THERAPY PROGRAM STATUS

RESTORE

PoC data in mouse

PoC preliminary data in Non-Human Primates

Product Development and Manufacturing Agreement

Next step: Advice from regulatory authorities

RESTORE

CONNEXIN 26 IS A GAP-JUNCTION PROTEIN ENCODED BY GJB2 GENE AND RESPONSIBLE FOR TISSUE HOMEOSTASIS MUTATIONS IN THE GENE LEADS TO DEAFNESS

- GJB2 is the gene encoding for the Connexin 26 protein; one of 20 known connexins in humans and almost endemic to the cochlea (together with Cx30); a hexamer of 6 proteins forms Gap Junctions
- Gap Junctions are key for the intercellular exchange of molecules (miRNA, glucose, ions, etc.) hence responsible for tissue homeostasis
- GJB2 cDNA = 681 bp compatible with the use of a **single AAV**
- More than 100 recessive mutations origin Cx26 truncation / deletion leading to non-syndromic hearing loss and deafness
- GJB2 mutations are the **most prevalent form of congenital deafness** (DFNB1).
- Children are usually being **diagnosed during the newborn screening** routine and current SoC is cochlear implantation prior language acquisition.
- Prof. Christine Petit observed in an epidemiology study that some patients demonstrating early onset of severe presbycusis carried GJB2 mutations.^[1]



Schematic representation of a gap junction – adapted from Kemperman, Hoefsloot and Cremers J R Soc Med 2002;95; 171-177

GJB2 HAS BEEN IDENTIFIED AS PART OF INSTITUT PASTEUR'S DELIBERATE AND SYSTEMATIC PROCESS TO IDENTIFY MONOGENIC FORMS OF EARLY ONSET OF SEVERE PRESBYCUSIS



- Severe presbycusis is a bilateral progressive loss of hearing starting from a high-frequency region of the hearing spectrum with an onset as early as 30-40 years old.
- Rare predicted pathogenic variants present in genes responsible for early onset forms of deafness explain 25% of all mARHL cases and 25% of sARHL cases. These mutations were not present in the normal population.
- Institut Pasteur's results establish the existence of a continuum of auditory phenotypes, from early-onset forms of deafness to severe presbycusis caused by mutations in the same set of genes.
- They indicate that many severe cases of presbycusis are likely monogenic disorders.

mARHL: family members presenting severe and early onset of presbycusis sARHL: subjects presenting the « worst » severe presbycusis phenotype AF: Allele Frequency



GJB2 GENE THERAPY PROGRAM NEXT STEPS

Natural history study

Candidate selection

Preclinical IND enabling studies

USH1G GENE ENCODES "SANS", AN ESSENTIAL PROTEIN FOR MECHANOELECTRICAL TRANSDUCTION





Adapted from Mathur and Yang. 2014

Tip links on top of hair cells are translating a vibration due to acoustic stimulation into electrical depolarization by mechanically opening ion channels



Adapted from Emptoz et al. 2017 (link)

The "sans" protein encoded by the USH1G gene is essential for the structural properties of the tip links

Sans protein

USH1G GENE THERAPY RESTORED HEARING & VESTIBULAR FUNCTIONS

PROOF OF CONCEPT IN A KNOCK-OUT MOUSE MODEL BY INSTITUT PASTEUR



Source: Emptoz *et al.*," Local gene therapy durably restores vestibular function in a mouse model of Usher syndrome type 1G," 2017 (link)

USH1G GENE THERAPY RESTORED HEARING & VESTIBULAR FUNCTIONS (CONT.)

PROOF OF CONCEPT IN A KNOCK-OUT MOUSE MODEL BY INSTITUT PASTEUR



Source: Emptoz et al. 2017 (link)

RESTORE

Restoration of stereocilia physiology using AAV8-SANS restored electrical excitability of sensory cells

RESTORE USH1G GENE THERAPY PROGRAM STATUS

PoC data in mouse



In progress: PoC data in mouse with an extended therapeutic window

Next step: PoC Non-Human Primates study

Next step: Advice from regulatory authorities

3 **SENS-401** TREAT **AND** PREVENT

SENS-401 MECHANISM OF ACTION CREATES THE OPPORTUNITY TO TARGET MULTIPLE INDICATIONS WITH ONE COMPOUND



SENS-401: MULTIPLE INDICATIONS PURSUED TO TREAT AND PREVENT HEARING LOSS

ORALLY AVAILABLE SMALL MOLECULE 5HT3 RECEPTOR ANTAGONIST & CALCINEURIN INHIBITOR – ESTIMATED TIMELINES

Indication	2020	20)21
Sudden Sensorineural Hearing Loss (SSNHL)*			Phase 2 read-out
Cisplatin induced ototoxicity (CIO)		Start of Natural History Study	Start of Clinical trial
Cell death post cochlear implant procedure		Cochlear*	Start of first clinical study of SENS- 401 in combination with cochlear implantation end of 2021/ beginning of 2022

* "Patriot" Consortium (IRBA, Sensorion, Echodia, Institut Pasteur) awarded up to €10.8m non dilutive financing by French government, staged over the duration of the project.

Sensorion will receive up to €5.6m to further develop SENS-401 in SSNHL French army participating in the ongoing Phase 2 study

SUDDEN SENSORINEURAL HEARING LOSS AND CISPLATIN INDUCED OTOTOXICITY CAN LEAD TO PERMANENT DISABLING HEARING LOSS

WHAT IS SSNHL?

The sudden onset of a significant hearing loss due to dysfunction of the cells of the cochlea and central auditory structures.

Hearing loss develops over less than 72 hrs, hearing sensitivity is reduced by at least 30 dB (1,000 fold) in the affected ear(s).

>70% of cases are idiopathic, known causes include noise/head trauma, ischemia, infection.

>50% of patients suffer from permanent disabling hearing loss, mostly those with initial severe/profound hearing loss.

Complications significantly impact quality of life due to:

- Difficulties in communicating, social isolation, cognitive decline
- Accompanying tinnitus

Incidence: 27-35 per 100,000 (218,000 patients in 2017 in G7 countries)¹

WHAT IS CIO?

Hearing loss caused by cisplatin administration as chemotherapeutic treatment. Risk factors include young age as well as individual and cumulative cisplatin doses.

CIO leads to permanent inner ear problems in 50-60% of cases. These complications significantly impact patients' quality of life due to:

- Hearing loss, tinnitus and dizziness impacting daily life activities
- Problems in language acquisition and learning for pediatric patients
- Difficulties in communicating, social isolation, cognitive decline

Potential treatments must not interfere with cisplatin efficacy

Incidence of Cisplatin treated patients: 500,000 patients in 2025 in G7 countries¹

¹ Company/ estimates based on publicly available data (in the US, Japan, Germany, France, the UK, Italy and Spain)

SENS-401 DEVELOPED TO TREAT SUDDEN SENSORINEURAL HEARING LOSS

SENS-401 DEMONSTRATED SAFETY IN PHASE 1

- 36 healthy volunteers enrolled in a double-blind, randomized, multiple ascending dose design (7 days)
- No serious or significant adverse event reported, safety profile comparable to placebo
- Pharmacokinetics match effective systemic exposures in preclinical model

SENS-401 MARKET EXCLUSIVITY

- Strong IP with 2 patent families
- Orphan Drug Designation from EMA
- Pediatric Investigation Plan approved in EU

TREAT

DAILY ADMINISTRATION OF SENS-401 REDUCES AUDITORY DEFICIT IN RATS

A daily oral administration of SENS-401 (13.2 mg/kg bid) reduces auditory deficit and improves recovery

ABR threshold recovery from 24h

MODEL

TREAT

 Randomized treatment post-noise induced trauma (2h exposure at 120 dB) in rats receiving either twice daily placebo or SENS-401 PO for 28 days

BENEFIT

- Regulatory threshold for efficacy (>10 dB improvement)
- Significant effects with treatment initiation delay up to 96 hrs



O placebo (n=7)

- SENS-401 from 24h (n=7) p<0.001</p>
- SENS-401 from 72h (n=8) p<0.012</p>
- SENS-401 from 96h (n=9) p<0.006</p>

Petremann et al. 2018

SENS-401 PHASE 2 TO TREAT SSNHL

A RANDOMIZED, MULTICENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL



*After review of the statistical analysis plan, an amendment to the study is currently under review by the regulatory authorities. Should it proceed satisfactorily, this would reduce significantly the sample size without compromising the quality and potential outcome of the trial.

TREAT

PREVENT SENS-401 PRE-CLINICAL PROOF OF CONCEPT IN CISPLATIN INDUCED HEARING LOSS

SIGNIFICANTLY REDUCES CISPLATIN-INDUCED HEARING LOSS AND OUTER HAIR CELL DEATH IN PRE-CLINICAL MODELS

TREATMENT PROTOCOL

SENS-401 6.6 mg/kg, 13.2 mg/kg or placebo were administered to rats once-daily for 13 consecutive days after cisplatin infusion

Auditory brainstem response (ABR) threshold shift at day 14

Cochleograms at day 14

Significantly more surviving outer hair cells were present after SENS-401 treatment compared with placebo (p<0.001), with up to 11-fold more in the basal turn of the cochlea

Significantimprovement versus placebo

23-28 dB with 6.6 mg/kg (p<0.010)

22-30 dB with 13.2 mg/kg (p<0.013)





Significant enhancement of Outer Hair Cells survival 22-264% for both doses

Source: Petremann *et al.* 2017, Otol Neurotol: Oral Administration of Clinical Stage Drug Candidate SENS-401 Effectively Reduces Cisplatin-induced Hearing Loss in Rats (link)

PREVENT COLLABORATION WITH COCHLEAR® LTD

COMBINATION OF COCHLEAR IMPLANT WITH SENS-401 TO PREVENT CELL-DEATH POST COCHLEAR IMPLANT PROCEDURE



²Market estimates (link)

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SENSORION

Potential Newsflow [Estimated timelines]

- Q1 2021 Final pre-clinical data for SENS-401 in cochlear implant study
- Mid-year 2021 Start of CIO Natural History Clinical Trial
- **Mid-year 2021** Ongoing approvals of the protocol amendment to reduce sample size for the SENS-401 Phase 2 study in SSNHL
- Mid-year 2021 Discussions with regulatory authorities on potential OTOF clinical study
- Mid-year 2021 Confirmatory pre-clinical PoC studies for USHER-GT
- H2 2021 Initiation of CIO Clinical Study in adults with SENS-401
- Q4 2021 Phase II readout from SENS-401 clinical study in SSNHL

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THANK YOU

Nawal Ouzren Chief Executive Officer E: contact@sensorion-pharma.com

